

PRELIMINARY AMENDMENT

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Serial No.: Unknown

Filed: Herewith

Title: USE OF HYALURONIC ACID OR ITS DERIVATIVES TO ENHANCE DELIVERY OF ANTINEOPLASTIC AGENTS

In the Claims

Please cancel claims 1-274 and add the following new claims 275-296:

Claims 1-274 (Canceled).

275. (New) A method of prophylactically or therapeutically treating a human suffering from a form of cancer, said method comprising:

- (1) directly injecting into a tumor in the human a non-toxic dosage amount of a pharmaceutical composition comprising:
 - (i) an anti-cancer drug and/or drug suitable for use to treat cancer, and
 - (ii) a form of hyaluronic acid selected from the group consisting of hyaluronic acid, pharmaceutically acceptable salts thereof, and combinations thereof, wherein the form of hyaluronic acid has a molecular weight less than 750,000 daltons and is in sterile water, and
- (2) administering systemically to the human, a non-toxic dosage amount of a pharmaceutical composition comprising:
 - (i) a form of hyaluronic acid selected from the group consisting of hyaluronic acid, pharmaceutically acceptable salts thereof, and combinations thereof,
 - (ii) a drug selected from the group consisting of:
 - (a) a non-steroidal anti-inflammatory drug (NSAID),
 - (b) a chemotherapeutic agent, and
 - (c) combinations thereof, and optionally
 - (iii) an anti-oxidant.

276. (New) The method of claim 275, wherein steps (1) and (2) are administered to the human one to four times monthly or more.

277. (New) The method of claim 275, wherein the form of cancer is breast cancer and steps (1) and (2) are administered to the human one to three times monthly or more.

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278. (New) The method of claim 275, wherein administering systemically is by intravenous administration.

279. (New) The method of claim 275, further comprising treating the human by hyperthermia.

280. (New) A method of prophylactically or therapeutically treating a human suffering from a form of cancer, said method comprising:

- (1) administering systemically to the human a first dosage amount of a pharmaceutical composition comprising a drug suitable for treating cancer, alone or in combination with a form of hyaluronic acid, selected from the group consisting of hyaluronic acid, pharmaceutically acceptable salts thereof, and combinations thereof, having a molecular weight of less than 750,000 daltons; and
- (2) administering systemically to the human a second dosage amount of a pharmaceutical composition comprising:
 - (i) a form of hyaluronic acid selected from the group consisting of hyaluronic acid, pharmaceutically acceptable salts thereof, and combinations thereof, having a molecular weight less than 750,000 daltons;
 - (ii) a drug selected from the group consisting of:
 - (a) a non-steroidal anti-inflammatory drug (NSAID),
 - (b) a chemotherapeutic agent, and
 - (c) combinations thereof, and, optionally
 - (iii) an anti-oxidant,

wherein the first and second dosage amounts are not the same and can be administered to the human sequentially or concomitantly.

281. (New) The method of treatment of claim 280, wherein steps (1) and (2) are repeated at least two times or more.

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282. (New) A method of prophylactically or therapeutically treating a human suffering from a metastatic form of cancer, said method of treatment comprising:

- (1) administering systemically to the human a first dosage amount of a pharmaceutical composition comprising a drug suitable for treating cancer, alone or in combination with a form of hyaluronic acid selected from the group consisting of hyaluronic acid, pharmaceutically acceptable salts thereof, and combinations thereof, having a molecular weight less than 750,000 daltons, and
- (2) administering systemically to the human a second dosage amount of a pharmaceutical composition comprising:
 - (i) a form of hyaluronic acid selected from the group consisting of hyaluronic acid, pharmaceutically acceptable salts thereof, and combinations thereof, having a molecular weight less than 750,000 daltons,
 - (ii) a drug selected from the group consisting of:
 - (a) a non-steroidal anti-inflammatory drug (NSAID);
 - (b) a chemotherapeutic agent, and
 - (c) combinations thereof, and optionally,
 - (iii) an anti-oxidant,

wherein said first and second dosage amounts are not the same, can be administered to the human sequentially or concomitantly, and can be administered to the human at regular intervals during a period of treatment.

283. (New) The method of treatment of claim 282, wherein steps (1) and (2) are administered to the human about 1-4 times monthly.

284. (New) A combination of dosage amounts of pharmaceutical compositions comprising:

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(1) a first non-toxic dosage amount of a pharmaceutical composition in a form for systemic administration to a human comprising:

- (i) a form of hyaluronic acid selected from the group consisting of hyaluronic acid, pharmaceutically acceptable salts thereof, and combinations thereof, having a molecular weight less than 750,000 daltons,
- (ii) a drug selected from the group consisting of:
 - (a) a non-steroidal anti-inflammatory drug (NSAID),
 - (b) a chemotherapeutic agent, and
 - (c) combinations thereof, and, optionally,
- (iii) an anti-oxidant; and

(2) a second non-toxic dosage amount of a pharmaceutical composition in a form for injection into a human comprising:

- (i) an anti-cancer drug and/or drug suitable for use to treat cancer, and
- (ii) a form of hyaluronic acid selected from the group consisting of hyaluronic acid, pharmaceutically acceptable salts thereof, and combinations thereof, wherein the form of hyaluronic acid has a molecular weight less than 750,000 daltons and is in sterile water, wherein the first and second non-toxic dosage amounts are not the same.

285. (New) The combination of claim 284, wherein the drug in the first dosage amount is an NSAID.

286. (New) The combination of claim 284, wherein the form of hyaluronic acid in the first and/or second non-toxic dosage amount is sodium hyaluronate.

287. (New) A method of prophylactically or therapeutically treating a human suffering from cancer, said method comprising:

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(1) directly injecting into a tumor in the human a non-toxic dosage amount of a pharmaceutical composition comprising novantrone and sodium hyaluronate in sterile water, said sodium hyaluronate having a molecular weight less than 750,000 daltons; and

(2) administering systemically to the human a non-toxic dosage amount of a pharmaceutical composition comprising:

- (i) sodium hyaluronate having a molecular weight less than 750,000 daltons,
- (ii) a drug selected from the group consisting of:
 - (a) diclofenac sodium,
 - (b) novantrone, and
 - (c) combinations thereof, and, optionally,
- (iii) Vitamin C.

288. (New) A combination of dosage amounts of pharmaceutical compositions comprising:

(1) a first non-toxic dosage amount of a pharmaceutical composition in a form for systemic administration to a human comprising

- (i) sodium hyaluronate having a molecular weight less than 750,000 daltons; and
- (ii) a drug selected from the group consisting of:
 - (a) diclofenac sodium,
 - (b) novantrone,
 - (c) combinations thereof, and, optionally,
- (iii) Vitamin C; and

(2) a second non-toxic dosage amount of a pharmaceutical composition for injection into a human comprising novantrone and/or a drug suitable for use to treat cancer and sodium hyaluronate in sterile water having a molecular weight less than 750,000 daltons.

289. (New) The method of claim 275, wherein the systemically administered form of hyaluronic acid is sodium hyaluronate having a molecular weight less than about 750,000 daltons.

290. (New) The method of claim 275, wherein steps (1) and (2) are repeated at least two times or more to prevent or reduce metastases.

291. (New) The method of claim 280, wherein the first dosage amount further comprises hyaluronic acid, pharmaceutically acceptable salts thereof, or combinations thereof, having a molecular weight less than 750,000 daltons.

292. (New) The method of claim 280, wherein the second dosage amount further comprises an anti-oxidant.

293. (New) A method of prophylactically or therapeutically treating a human suffering from a metastatic form of cancer, said method of treatment comprising:

(1) directly injecting into a tumor in the human a non-toxic dosage amount of a pharmaceutical composition comprising:

- (i) an anti-cancer drug and/or drug suitable for use to treat cancer, and
- (ii) a form of hyaluronic acid selected from the group consisting of hyaluronic acid, pharmaceutically acceptable salts thereof, and combinations thereof, wherein the form of hyaluronic acid has a molecular weight less than 750,000 daltons and is in sterile water, and

(2) administering systemically to the human, a non-toxic dosage amount of a pharmaceutical composition comprising:

- (i) a form of hyaluronic acid selected from the group consisting of hyaluronic acid, pharmaceutically acceptable salts thereof, and combinations thereof,
- (ii) a drug selected from the group consisting of:
 - (a) a non-steroidal anti-inflammatory drug (NSAID),

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- (b) a chemotherapeutic agent, and
- (c) combinations thereof, and optionally
- (iii) an anti-oxidant.

294. (New) The method of claim 293, wherein steps (1) and (2) are administered to the human one to four times monthly, or more.

295. (New) The method of claim 282, wherein the first dosage amount further comprises hyaluronic acid, pharmaceutically acceptable salts thereof, or combinations thereof, having a molecular weight less than 750,000 daltons.

296. (New) The method of claim 282, wherein the second dosage amount further comprises an anti-oxidant.